

R<sup>3</sup> is hydrogen, a functional group, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted alkoxy, optionally substituted aralkyl, optionally substituted aralkyloxy, optionally substituted cycloalkyl;

5 R<sup>4</sup> is a group NHCOR<sup>15</sup>, NHSO<sub>2</sub>R<sup>15</sup> or OCONR<sup>16</sup>R<sup>17</sup> where R<sup>15</sup> is optionally substituted alkyl, optionally substituted aryl or optionally substituted heteroaryl and R<sup>16</sup> and R<sup>17</sup> are independently selected from hydrogen, optionally substituted alkyl, optionally substituted aryl and optionally substituted heteroaryl, with the proviso that at least one of R<sup>16</sup> or R<sup>17</sup> is other than hydrogen, or R<sup>16</sup> and R<sup>17</sup> together with the nitrogen atom to which they

10 are attached form an optionally substituted heterocyclic ring which optionally contains further heteroatoms; and

R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are independently selected from hydrogen, a functional group or an optionally substituted hydrocarbyl groups or optionally substituted heterocyclic groups.

Suitably, where R<sup>4</sup> is a group NHCOR<sup>15</sup>, R<sup>15</sup> is substituted alkyl, optionally substituted aryl or optionally substituted heteroaryl.

Compounds of formula (I) are inhibitors of monocyte chemoattractant protein-1. In addition, they appear to inhibit RANTES (Regulated upon Activation, Normal T-cell Expressed and Secreted), induced chemotaxis. RANTES is another chemokine from the same family as MCP-1, with a similar biological profile, but acting through the CCR1 receptor. As a result, these compounds can be used to treat disease mediated by these agents, in particular inflammatory disease.

In this specification the term 'alkyl' when used either alone or as a suffix includes straight chained, branched structures. These groups may contain up to 10, preferably up to 6 and more preferably up to 4 carbon atoms. Similarly the terms "alkenyl" and "alkynyl" refer to unsaturated straight or branched structures containing for example from 2 to 10, preferably from 2 to 6 carbon atoms. Cyclic moieties such as cycloalkyl, cycloalkenyl and cycloalkynyl are similar in nature but have at least 3 carbon atoms. Terms such as "alkoxy" comprise alkyl groups as is understood in the art.

The term "halo" includes fluoro, chloro, bromo and iodo. References to aryl groups include aromatic carbocyclic groups such as phenyl and naphthyl. The term "heterocyclyl" includes aromatic or non-aromatic rings, for example containing from 4 to 20, suitably from 5 to 8 ring atoms, at least one of which is a heteroatom such as oxygen, sulphur or nitrogen.

Examples of such groups include furyl, thienyl, pyrrolyl, pyrrolidinyl, imidazolyl, triazolyl, thiazolyl, tetrazolyl, oxazolyl, isoxazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, quinolinyl, isoquinolinyl, quinoxaliny, benzothiazolyl, benzoxazolyl, benzothienyl or benzofuryl.

5 "Heteroaryl" refers to those groups described above which have an aromatic character. The term "aralkyl" refers to aryl substituted alkyl groups such as benzyl.

Other expressions used in the specification include "hydrocarbyl" which refers to any structure comprising carbon and hydrogen atoms. For example, these may be alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkoxy, aralkyl, cycloalkyl, cycloalkenyl or cycloalkynyl.

10 The term "functional group" refers to reactive substituents. They may comprise electron-donating or electron-withdrawing. Examples of such groups include halo, cyano, nitro,  $C(O)_nR^{18}$ ,  $OR^{18}$ ,  $S(O)_nR^{18}$ ,  $NR^{19}R^{20}$ ,  $C(O)NR^{19}R^{20}$ ,  $OC(O)NR^{19}R^{20}$ ,  $-NR^{19}C(O)_nR^{18}$ ,  $-NR^{18}CONR^{19}R^{20}$ ,  $-N=CR^{19}R^{20}$ ,  $S(O)_mNR^{19}R^{20}$  or  $-NR^{19}S(O)_nR^{18}$  where  $R^{18}$ ,  $R^{19}$  and  $R^{20}$  are independently selected from hydrogen or optionally substituted hydrocarbyl, or  $R^{19}$  and  $R^{20}$  15 together form an optionally substituted ring which optionally contains further heteroatoms such as  $S(O)_m$ , oxygen and nitrogen,  $n$  is an integer of 1 or 2,  $m$  is 1 or 2.

Suitable optional substituents for hydrocarbyl groups  $R^{18}$ ,  $R^{19}$  and  $R^{20}$  include halo, perhaloalkyl such as trifluoromethyl, mercapto, hydroxy, carboxy, alkoxy, heteroaryl, heteroaryloxy, alkenyloxy, alkynyoxy, alkoxyalkoxy, aryloxy (where the aryl group may be substituted by halo, nitro, or hydroxy), cyano, nitro, amino, mono- or di-alkyl amino, oximino or  $S(O)_nR^x$  where  $n$  is as defined above and  $R^x$  is alkyl such as  $C_{1-4}$  alkyl.

Suitable substituents for these hydrocarbyl or heterocyclic groups include those listed above for  $R^{18}$ ,  $R^{19}$  and  $R^{20}$ .

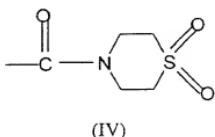
25 Suitably  $R^1$  is an optionally substituted phenyl, pyridyl, naphthyl, furyl or thienyl ring, and in particular is a substituted phenyl or pyridyl ring.

Suitable optional substituents for  $R^1$  in formula (I) include alkyl, alkenyl, alkynyl, halo, perhaloalkyl including trifluoromethyl, mercapto, alkoxy, haloalkoxy, alkenyloxy, alkynyoxy, hydroxyalkoxy, alkoxyalkoxy, alkanoyl, alkanoyloxy, cyano, nitro, amino, mono- or di-alkyl amino, oximino, sulphonamido, carbamoyl, mono or 30 dialkylcarbamoyl or  $S(O)_mR^{21}$  where  $m$  is as defined above and  $R^{21}$  is hydrocarbyl.

Particular examples of substituents  $R^5$ ,  $R^6$  and  $R^7$ , and where appropriate also  $R^4$  include hydrogen, hydroxy, halo, optionally substituted alkyl such as aralkyl, carboxyalkyl or

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the amide derivative thereof; alkoxy; aryloxy; aralkyloxy; or an amino group which is optionally substituted with alkyl, aryl or aralkyl. A specific functional group which is suitable for R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and/or R<sup>7</sup> is a group of sub-formula (IV).



Particular examples of groups R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> are hydrogen, hydroxy, halo or alkoxy.

In particular R<sup>6</sup> and R<sup>7</sup> are hydrogen. R<sup>5</sup> may be hydrogen but in addition is suitably a small 10 substituent such as hydroxy, halo or methoxy.

Particular substituents for R<sup>1</sup> include trifluoromethyl, C<sub>1-4</sub>alkyl, halo, trifluoromethoxy, C<sub>1-4</sub>alkoxy, C<sub>1-4</sub>alkanoyl, C<sub>1-4</sub>alkanoyloxy, nitro, carbamoyl, C<sub>1-4</sub>alkoxycarbonyl, C<sub>1-4</sub>alkylsulphonyl, C<sub>1-4</sub>alkylsulphonyl, C<sub>1-4</sub>alkylsulphonyl, sulphonamido, carbamoylC<sub>1-4</sub>alkyl, N-(C<sub>1-4</sub>alkyl)carbamoylC<sub>1-4</sub>alkyl, N-(C<sub>1-4</sub>alkyl)<sub>2</sub>carbamoyl-C<sub>1-4</sub>alkyl, 15 hydroxyC<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkoxyC<sub>1-4</sub>alkyl.

Additionally or alternatively, two such substituents together may form a divalent radical of the formula -O(CH<sub>2</sub>)<sub>1-4</sub>O- attached to adjacent carbon atoms on the R<sup>1</sup> ring.

Preferred substituents for R<sup>1</sup> are one or more non-polar substituents such as halo.

In particular, R<sup>1</sup> is substituted by one or more halo groups, in particular chlorine. A 20 particular example of an R<sup>1</sup> group is 3,4-dichlorophenyl, 3-fluoro-4-chlorophenyl, 3-chloro-4-fluorophenyl or 2,3-dichloropyrid-5-yl.

Examples of groups R<sup>2</sup> include carboxy; cyano; tetrazol-5-yl; SO<sub>2</sub>H; -CONHR<sup>8</sup> where R<sup>8</sup> is selected from cyano, hydroxy, -SO<sub>2</sub>R<sup>12</sup> where R<sup>12</sup> is alkyl such as C<sub>1-4</sub>alkyl, aryl such as phenyl, heteroaryl or trifluoromethyl, or R<sup>8</sup> is a group -(CHR<sup>10</sup>)-COOH where r is an integer of 25 1-3 and each R<sup>10</sup> group is independently selected from hydrogen or alkyl such as C<sub>1-4</sub>alkyl; or R<sup>2</sup> is a group -SO<sub>2</sub>NHR<sup>9</sup> where R<sup>9</sup> is an optionally substituted phenyl or an optionally substituted 5 or 6 membered heteroaryl group, or a group COR<sup>14</sup> where R<sup>14</sup> is alkyl such as C<sub>1-4</sub>alkyl, aryl such as phenyl, heteroaryl or trifluoromethyl, or R<sup>2</sup> is a group of formula (VI)